Pre-filled Columns for Flash Chromatography Higher Separating Power.

BACKGROUND OF THE INVENTION

Field of the invention.

The present invention relates to pre-filled columns for flash chromatography. These columns, which are filled with spherical and porous silica gel or with semi-spherical and porous silica gel, allow a considerable increase in the quality of the purification of synthetic products by means of flash chromatography.

The technique of flash chromatography can particularly be applied to the fast purification under low and medium pressure of synthetic products in pharmaceutical, cosmetic, agro-chemical and biotechnology research.

State of the art of flash chromatography

The technique of chromatography was discovered more than 100 years ago by a Russian chemist named TSWETT. This chemist described the separating power of alumina oxide placed in a glass column on which he deposited chlorophyll. He observed the descending migration of color rings along the glass column.

Since his discovery, numerous analytical, preparative, and industrial applications have been developed.

Gas chromatography (GC) and high performance liquid chromatography (HPLC) can be cited as being among the most important applications. Flash chromatography was born from the need to purify synthetic products rapidly and simply in a laboratory context and in quantities comprised between 10 mg to 100 g.

Flash chromatography differs from preparative HPLC in the granularity of the silica gel, namely the granules are bigger in flash chromatography, and provide a simpler and more rapid application of flash chromatography.

Pre-filled flash chromatography columns filled with irregular porous silica gel and with granules of 40-60 μm or 20-40 μm, have been on the market for several years. These new chromatography columns brought an enhanced ease of use through immediate application. However, these columns did not bring any advantage in terms of the quality of separation.

SUMMARY OF THE INVENTION

In the invention described herein, the separating properties of flash chromatography columns have been increased significantly, while maintaining the ease of use of the technique combined with a low working counter-pressure.

DETAILED DESCRIPTION OF THE INVENTION

According to one aspect of the invention, there are provided columns for flash chromatography with spherical and porous silica gel that have granules comprised between 3 and 45μm and pores comprised between 30 and 300 Å. According to another aspect of the invention, there are provided columns for flash chromatography with semi-spherical and porous silica gel having granules comprised between 3 and 45 μm and pores comprised between 30 and 300 Å.

A pre-filled column for flash chromatography is manufactured by filling a tube or a syringe or any other suitable body, on which a frit (filter) is attached to prevent the silica gel from leaving.
A quantity of spherical and porous silica gel or of semi-spherical and porous silica gel is poured.
A second frit is then placed with force on top of the bed that has been created.
In order to have good homogeneity in the filling of the tube, syringe or other suitable body and to eliminate preferential paths that are detrimental to the technique, the column is made to vibrate while, at the same time, the upper frit is pushed by means of an appropriate object so as to achieve a homogenous compression on the entire surface of the frit.
A homogenous packing can also be obtained though use of liquids or gasses.
After the dead volume has been reabsorbed, the flash chromatography column is ready for use.
It is possible to improve the quality of the compression by passing a solvent through the column until the upper bed of the column has stabilized.

Example 1: A column for flash chromatography is manufactured with 50 g of spherical and porous silica gel having granules of 25-40μm.

Column length: 85 mm.
Silica gel: 50 g of spherical and porous silica gel of 70Å pore size.
Recipient: syringe body of 150 ml volume and a diameter of 37 mm

Take the 150 ml syringe body and place a porous frit in the bottom of the syringe body.
Pour 50 g of spherical and porous silica gel in the column.
Add a second porous frit on top of silica bed.
Press on the top frit while vibrating the whole with vibrator or a vibrating table.
Wait until the bed has stabilized and does not move downwards.

a) Results obtained

Operational conditions:
Eluent: Ethyl acetate/ Hexane.
Flow: 35ml/min.
Detection: UV 254 mn
Gradient: A: Hexane / B: Ethyl acetate.

FIG. 1 illustrates the main substance that has been injected.

FIG. 2. illustrates

Time	% A	% B
0	100	0
5	100	0
5.1	90	10
10	90	10
10.1	80	20
15.0	80	20
15.1	70	30
25	70	30

the chromatogram obtained.

Number of plates on the main peak: 684.
K´: 10.
Working pressure: 16 psi.
Asymmetry of main peak: 1.75.

FIG. 3 shows, for the purpose of comparison, a chromatogram of a same column and in the same conditions, but filled with irregular silica gel, granules of 15-35 µm, in accordance with the prior art.

Number of plates of the main peak: 156.
K´: 10.5.
Working pressure: 43 psi.
Asymmetry of main peak: 5.88.

c) Comparative table

	Column with spherical and porous silica gel	Column with irregular and porous silica gel
Number of plates	684	156
K'	10	10.5
Working pressure	16 psi	43 psi
Asymmetry of the main peak	1.75	5.88

Although specific embodiments of the invention have been described and illustrated, the invention is not to be limited to the specific forms or arrangements of parts so described and illustrated. The invention is limited only by the claims.